CLAIMS

Claims 1-54 (cancelled).

Add new claims 55-78.

55. (new) A controlled release methylphenidate tablet comprising:

(A) an immediate release methylphenidate coating comprising;

(a) methylphenidate or a pharmaceutically acceptable salt or isomer thereof ;

(b) a binder; and

(c) optionally a stabilizer;

(B) a controlled release methylphenidate core tablet comprising:

(a) a compressed mixture comprising:

(i) methylphenidate or a pharmaceutically acceptable salt or isomer thereof;

(ii) 1 to about 50% of the total weight of the compressed mixture of a hydrogel polymer; and

(iii) a diluent; and

(b) an enteric coating surrounding the compressed mixture comprising;

(i) 45-80 weight percent based upon the total weight of the enteric coating of at least one enteric polymer; and

(ii) at least one conventional processing aid; and

(C) optionally an aesthetic coating

wherein the controlled release methylphenidate tablet exhibits the following dissolution profile when tested in a United States Pharmacopoeia type 2 (paddle) apparatus at 50 rpms in 900 ml of phosphate buffer with a pH of 7.5 and at 37°C:

1-35% of the methylphenidate is released after 1 hour;

5-40% of the methylphenidate is released after 2 hours; and

not less than 70% is release after 10 hours and when administered to humans exhibits a plasma peak for the immediate release layer (T_{max1}) between 1 and 5 hours, a plasma peak for the controlled release core (T_{max2}) between 4 and 12 hours, and a plasma trough (T_{min}) between 2 and

7 hours in between the two peak plasma levels; and

wherein said tablet exhibits an in vitro curve similar to that shown in Figure 4.

56. (new) The controlled release methylphenidate tablet as defined in claim 55 wherein the hydrogel polymer in the compressed mixture is selected from the group consisting of methyl cellulose, hydroxymethyl cellulose, polyvinyl pyrrolidone, hydroxyethyl cellulose, hydroxypropyl cellulose, hydroxypropyl methylcellulose, polyethylene oxides, gums, acrylate polymers and methacrylate polymers.

57. (new) The controlled release methylphenidate tablet as defined in claim 55 wherein the enteric polymer is selected from a group consisting of zein, methacrylic acid copolymers, cellulose acetate phthalate, hydroxypropyl methylcellulose phthalate, hydroxypropyl methylcellulose acetate succinate, cellulose acetate trimellitate, shellac, polyvinyl acetate phthalate or mixtures thereof.

58. (new) The controlled release methylphenidate tablet as defined in claim 55 wherein the T_{max1} occurs less than 3 hours and declines in less than 5 hours.

59. (new) The controlled release methylphenidate tablet as defined in claim 55 wherein the T_{max2} occurs about 7 to 9 hours and declines to about 1.4 ng/ml in about 14 to 18 hours.

60. (new) A controlled release methylphenidate tablet as defined in claim 55 consisting essentially of:

(A) an immediate release methylphenidate coating consisting essentially of;

(a) 30-60 weight percent based upon the total weight of the immediate release coating of methylphenidate or a pharmaceutically acceptable salt or isomer thereof ;

(b) 40-70 weight percent based upon the total weight of the immediate release coating of a binder; and

(c) 0.005-5 weight percent based upon the total weight of the immediate release coating of a stabilizer;

(B) a controlled release methylphenidate core tablet consisting essentially of:

(a) a compressed mixture consisting essentially of:

(i) 5-40 weight percent based upon the total weight of the compressed mixture of methylphenidate or a pharmaceutically acceptable salt or isomer thereof;

(ii) 3-40 weight percent based upon the total weight of the compressed mixture of a hydrogel polymer;

(iii) 25-90 weight percent based upon the total weight of the compressed mixture of a diluent; and

(iv) 0.1-10 weight percent based upon the total weight of the compressed mixture of an anti-sticking agent; and

(b) an enteric coating surrounding the core tablet consisting essentially of;

(i) 45-80 weight percent based upon the total weight of the enteric coating of at least one enteric polymer;

(ii) 0.5-15 weight percent based upon the total weight of the enteric coating of a plasticizer; and

(iii) an anti-sticking agent; and

(C) optionally an aesthetic coating

wherein the controlled release methylphenidate tablet exhibits the following dissolution profile when tested in a United States Pharmacopeia type 2 (paddle) apparatus at 50 rpms in 900 ml of phosphate buffer with a pH of 7.5 and at 37°C:

1-35% of the methylphenidate is released after 1 hour;

5-40% of the methylphenidate is released after 2 hours; and

not less than 70% is release after 10 hours and when administered to humans exhibits a plasma peak for the immediate release layer (T_{max1}) between 1 and 5 hours, a plasma peak for the controlled release core (T_{max2}) between 4 and 12 hours, and a plasma trough (T_{min}) between 2 and 7 hours in between the two peak plasma levels.

61. (new) The controlled release methylphenidate tablet as defined in claim 60 wherein:

(A) the immediate release methylphenidate coating consists essentially of;

(a) 40-50 weight percent based upon the total weight of the immediate release coating of methylphenidate or a pharmaceutically acceptable salt or isomer thereof ;

(b) 45-60 weight percent based upon the total weight of the immediate release

coating of a binder; and

(c) 0.01-2 weight percent based upon the total weight of the immediate release coating of a stabilizer;

(B) the controlled release methylphenidate core tablet consists essentially of:

(a) a compressed mixture consisting essentially of:

(i) 10-25 weight percent based upon the total weight of the compressed mixture of methylphenidate or a pharmaceutically acceptable salt or isomer thereof;

(ii) 3-40 weight percent based upon the total weight of the compressed mixture of a hydrogel polymer;

(iii) 45-85 weight percent based upon the total weight of the compressed mixture of a diluent; and

(iv) 0.5-5 weight percent based upon the total weight of the compressed mixture of an anti-sticking agent; and

(b) an enteric coating surrounding the core tablet consisting essentially of;

(i) 45-80 weight percent based upon the total weight of the enteric coating of at least one enteric polymer;

(ii) 1-5 weight percent based upon the total weight of the enteric coating of a plasticizer; and

(iii) an anti-sticking agent.

62. (new) A controlled release methylphenidate tablet comprising:

(A) an immediate release methylphenidate coating comprising;

(a) methylphenidate or a pharmaceutically acceptable salt or isomer thereof ;

(b) a binder; and

(c) optionally a stabilizer;

(B) a controlled release methylphenidate core tablet comprising:

(a) a compressed mixture comprising:

(i) methylphenidate or a pharmaceutically acceptable salt or isomer thereof;

(ii) 1 to about 50% of the total weight of the compressed mixture of a hydrogel polymer; and

(iii) a diluent; and

(b) an enteric coating surrounding the compressed mixture comprising;

(i) 45-80 weight percent based upon the total weight of the enteric coating of at least one enteric polymer; and

(ii) at least one conventional processing aid; and

(C) optionally an aesthetic coating

wherein the controlled release methylphenidate tablet exhibits the following dissolution profile when tested in a United States Pharmacopoeia type 2 (paddle) apparatus at 50 rpms in 900 ml of phosphate buffer with a pH of 7.5 and at 37°C:

1-35% of the methylphenidate is released after 1 hour;

5-40% of the methylphenidate is released after 2 hours; and

not less than 70% is release after 10 hours and when administered to humans exhibits a plasma peak for the immediate release layer (T_{max1}) between 1 and 5 hours, a plasma peak for the controlled release core (T_{max2}) between 4 and 12 hours, and a plasma trough (T_{min}) between 2 and 7 hours in between the two peak plasma levels; and

wherein said tablet exhibits an in vitro curve similar to that shown in Figure 5.

63. (new) The controlled release methylphenidate tablet as defined in claim 62 wherein the controlled release tablet releases 42-53% of the methylphenidate after 4 hours of testing in a United States Pharmacopoeia type 1 apparatus at 100 rpms in 500 ml of phosphate buffer with a pH of 7.5 and at 37°C.

64. (new) The controlled release methylphenidate tablet as defined in claim 62 wherein the controlled release tablet releases 67-81% of the methylphenidate after 6 hours of testing in a United States Pharmacopoeia type 1 apparatus at 100 rpms in 500 ml of phosphate buffer with a pH of 7.5 and at 37°C.

65. (new) The controlled release methylphenidate tablet as defined in claim 62 wherein the hydrogel polymer in the compressed mixture is selected from the group consisting of methyl cellulose, hydroxymethyl cellulose, polyvinyl pyrrolidone, hydroxyethyl cellulose, hydroxypropyl cellulose,

hydroxypropyl methylcellulose, polyethylene oxides, gums, acrylate polymers and methacrylate polymers.

66. (new) The controlled release methylphenidate tablet as defined in claim 62 wherein the enteric polymer is selected from a group consisting of zein, methacrylic acid copolymers, cellulose acetate phthalate, hydroxypropyl methylcellulose phthalate, hydroxypropyl methylcellulose acetate succinate, cellulose acetate trimellitate, shellac, polyvinyl acetate phthalate or mixtures thereof.

67. (new) The controlled release methylphenidate tablet as defined in claim 62 wherein the T_{max1} occurs less than 3 hours and declines in less than 5 hours.

68. (new) The controlled release methylphenidate tablet as defined in claim 62 wherein the T_{max2} occurs about 7 to 9 hours and declines to about 1.4 ng/ml in about 14 to 18 hours.

69. (new) A controlled release methylphenidate tablet as defined in claim 62 consisting essentially of:

(A) an immediate release methylphenidate coating consisting essentially of;

(a) 30-60 weight percent based upon the total weight of the immediate release coating of methylphenidate or a pharmaceutically acceptable salt or isomer thereof ;

(b) 40-70 weight percent based upon the total weight of the immediate release coating of a binder; and

(c) 0.005-5 weight percent based upon the total weight of the immediate release coating of a stabilizer;

(B) a controlled release methylphenidate core tablet consisting essentially of:

(a) a compressed mixture consisting essentially of:

(i) 5-40 weight percent based upon the total weight of the compressed mixture of methylphenidate or a pharmaceutically acceptable salt or isomer thereof;

(ii) 3-40 weight percent based upon the total weight of the compressed mixture of a hydrogel polymer;

(iii) 25-90 weight percent based upon the total weight of the compressed mixture of a diluent; and

(iv) 0.1-10 weight percent based upon the total weight of the compressed mixture of an anti-sticking agent; and

(b) an enteric coating surrounding the core tablet consisting essentially of;

(i) 45-80 weight percent based upon the total weight of the enteric coating of at least one enteric polymer;

(ii) 0.5-15 weight percent based upon the total weight of the enteric coating of a plasticizer; and

(iii) an anti-sticking agent; and

(C) optionally an aesthetic coating

wherein the controlled release methylphenidate tablet exhibits the following dissolution profile when tested in a United States Pharmacopeia type 2 (paddle) apparatus at 50 rpms in 900 ml of phosphate buffer with a pH of 7.5 and at 37°C:

1-35% of the methylphenidate is released after 1 hour; 5-40% of the methylphenidate is released after 2 hours; and not less than 70% is release after 10 hours and when administered to humans exhibits a plasma peak for the immediate release layer (T_{max1}) between 1 and 5 hours, a plasma peak for the controlled release core (T_{max2}) between 4 and 12 hours, and a plasma trough (T_{min}) between 2 and 7 hours in between the two peak plasma levels.

70. (new) The controlled release methylphenidate tablet as defined in claim 69 wherein:

(A) the immediate release methylphenidate coating consists essentially of;

(a) 40-50 weight percent based upon the total weight of the immediate release coating of methylphenidate or a pharmaceutically acceptable salt or isomer thereof ;

(b) 45-60 weight percent based upon the total weight of the immediate release coating of a binder; and

(c) 0.01-2 weight percent based upon the total weight of the immediate release coating of a stabilizer;

(B) the controlled release methylphenidate core tablet consists essentially of:

(a) a compressed mixture consisting essentially of:

(i) 10-25 weight percent based upon the total weight of the compressed mixture of methylphenidate or a pharmaceutically acceptable salt or isomer thereof;

(ii) 3-40 weight percent based upon the total weight of the compressed mixture of a hydrogel polymer;

(iii) 45-85 weight percent based upon the total weight of the compressed mixture of a diluent; and

(iv) 0.5-5 weight percent based upon the total weight of the compressed mixture of an anti-sticking agent; and

(b) an enteric coating surrounding the core tablet consisting essentially of;

(i) 45-80 weight percent based upon the total weight of the enteric coating of at least one enteric polymer;

(ii) 1-5 weight percent based upon the total weight of the enteric coating of a plasticizer; and

(iii) an anti-sticking agent.

71. (new) A controlled release methylphenidate tablet comprising:

(A) an immediate release methylphenidate coating comprising;

(a) methylphenidate or a pharmaceutically acceptable salt or isomer thereof ;

(b) a binder; and

(c) optionally a stabilizer;

(B) a controlled release methylphenidate core tablet comprising:

(a) a compressed mixture comprising:

(i) methylphenidate or a pharmaceutically acceptable salt or isomer thereof;

(ii) 1 to about 50% of the total weight of the compressed mixture of a hydrogel polymer; and

(iii) a diluent; and

(b) an enteric coating surrounding the compressed mixture comprising;

(i) 45-80 weight percent based upon the total weight of the enteric coating of at least one enteric polymer; and

(ii) at least one conventional processing aid; and

(C) optionally an aesthetic coating

wherein the controlled release methylphenidate tablet exhibits the following dissolution profile when

tested in a United States Pharmacopoeia type 2 (paddle) apparatus at 50 rpms in 900 ml of phosphate buffer with a pH of 7.5 and at 37°C:

1-35% of the methylphenidate is released after 1 hour; 5-40% of the methylphenidate is released after 2 hours; and not less than 70% is release after 10 hours and when administered to humans exhibits a plasma peak for the immediate release layer (T_{max1}) between 1 and 5 hours, a plasma peak for the controlled release core (T_{max2}) between 4 and 12 hours, and a plasma trough (T_{min}) between 2 and 7 hours in between the two peak plasma levels; and

wherein said tablet exhibits an in vitro curve similar to that shown in Figure 6.

72. (new) The controlled release methylphenidate tablet as defined in claim 71 wherein the controlled release tablet releases 67-81% of the methylphenidate after 6 hours of testing in a United States Pharmacopoeia type 1 apparatus at 100 rpms in 500 ml of phosphate buffer with a pH of 7.5 and at 37°C.

73. (new) The controlled release methylphenidate tablet as defined in claim 71 wherein the hydrogel polymer in the compressed mixture is selected from the group consisting of methyl cellulose, hydroxymethyl cellulose, polyvinyl pyrrolidone, hydroxyethyl cellulose, hydroxypropyl cellulose, hydroxypropyl methylcellulose, polyethylene oxides, gums, acrylate polymers and methacrylate polymers.

74. (new) The controlled release methylphenidate tablet as defined in claim 71 wherein the enteric polymer is selected from a group consisting of zein, methacrylic acid copolymers, cellulose acetate phthalate, hydroxypropyl methylcellulose phthalate, hydroxypropyl methylcellulose acetate succinate, cellulose acetate trimellitate, shellac, polyvinyl acetate phthalate or mixtures thereof.

75. (new) The controlled release methylphenidate tablet as defined in claim 71 wherein the T_{max1} occurs less than 3 hours and declines in less than 5 hours.

76. (new) The controlled release methylphenidate tablet as defined in claim 71 wherein the T_{max2} occurs about 7 to 9 hours and declines to about 1.4 ng/ml in about 14 to 18 hours.

77. (new) A controlled release methylphenidate tablet as defined in claim 71 consisting essentially of:

(A) an immediate release methylphenidate coating consisting essentially of;

(a) 30-60 weight percent based upon the total weight of the immediate release coating of methylphenidate or a pharmaceutically acceptable salt or isomer thereof ;

(b) 40-70 weight percent based upon the total weight of the immediate release coating of a binder; and

(c) 0.005-5 weight percent based upon the total weight of the immediate release coating of a stabilizer;

(B) a controlled release methylphenidate core tablet consisting essentially of:

(a) a compressed mixture consisting essentially of:

(i) 5-40 weight percent based upon the total weight of the compressed mixture of methylphenidate or a pharmaceutically acceptable salt or isomer thereof;

(ii) 3-40 weight percent based upon the total weight of the compressed mixture of a hydrogel polymer;

(iii) 25-90 weight percent based upon the total weight of the compressed mixture of a diluent; and

(iv) 0.1-10 weight percent based upon the total weight of the compressed mixture of an anti-sticking agent; and

(b) an enteric coating surrounding the core tablet consisting essentially of;

(i) 45-80 weight percent based upon the total weight of the enteric coating of at least one enteric polymer;

(ii) 0.5-15 weight percent based upon the total weight of the enteric coating of a plasticizer; and

(iii) an anti-sticking agent; and

(C) optionally an aesthetic coating

wherein the controlled release methylphenidate tablet exhibits the following dissolution profile when tested in a United States Pharmacopeia type 2 (paddle) apparatus at 50 rpms in 900 ml of phosphate buffer with a pH of 7.5 and at 37°C:

1-35% of the methylphenidate is released after 1 hour; 5-40% of the methylphenidate is released

after 2 hours; and not less than 70% is release after 10 hours and when administered to humans exhibits a plasma peak for the immediate release layer (T_{max1}) between 1 and 5 hours, a plasma peak for the controlled release core (T_{max2}) between 4 and 12 hours, and a plasma trough (T_{min}) between 2 and 7 hours in between the two peak plasma levels.

78. (new) The controlled release methylphenidate tablet as defined in claim 77 wherein:

(A) the immediate release methylphenidate coating consists essentially of;

(a) 40-50 weight percent based upon the total weight of the immediate release coating of methylphenidate or a pharmaceutically acceptable salt or isomer thereof ;

(b) 45-60 weight percent based upon the total weight of the immediate release coating of a binder; and

(c) 0.01-2 weight percent based upon the total weight of the immediate release coating of a stabilizer;

(B) the controlled release methylphenidate core tablet consists essentially of:

(a) a compressed mixture consisting essentially of:

(i) 10-25 weight percent based upon the total weight of the compressed mixture of methylphenidate or a pharmaceutically acceptable salt or isomer thereof;

(ii) 3-40 weight percent based upon the total weight of the compressed mixture of a hydrogel polymer;

(iii) 45-85 weight percent based upon the total weight of the compressed mixture of a diluent; and

(iv) 0.5-5 weight percent based upon the total weight of the compressed mixture of an anti-sticking agent; and

(b) an enteric coating surrounding the core tablet consisting essentially of;

(i) 45-80 weight percent based upon the total weight of the enteric coating of at least one enteric polymer;

(ii) 1-5 weight percent based upon the total weight of the enteric coating of a plasticizer; and

(iii) an anti-sticking agent.